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EXAMINER	
KAPUSHOC, STEPHEN THOMAS	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/824,656	Applicant(s) FRANZEN ET AL.	
	Examiner Stephen Kapushoc	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 06 February 2007.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1,4-8 and 11-19 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,4-8 and 11-19 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 2, 3, 9, and 10 are cancelled'
Claims 1, 4-8, 11-19 pending and examined on the merits.

This Office Action is in reply to Applicants' correspondence of 02/06/2007. Claim(s) 2, 3, 9, and 10 is/are cancelled; no claim(s) is/are withdrawn; no claim(s) has/have been newly added; claim(s) 1, 4-8, 11, 13-16, 18, and 19 has/have been amended.

Applicants' remarks and amendments have been fully and carefully considered but are not found to be sufficient to put the application in condition for allowance. Any new objections or grounds of rejection presented in this Office Action are necessitated by Applicants amendments. Any rejections or objections not reiterated herein have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.

This Action is made **FINAL.**

Response to Remarks Regarding the Teachings of Knoll (1999; WO 99/27367) and the Required limitations of the Claims

Applicants have traversed (e.g. Remarks of 02/06/2007, p.9) the rejection of claims in view of the teachings of Knoll (WO 99/27367). Rejections of the claims are set forth and maintained in this Office Action. Applicants argue that:

> In accordance with one embodiment of the invention described in paragraphs [18] and [44] to [46] a galvanic element is constructed by binding nanoparticles with a metal surface to probe molecules, adding an electrolyte, and contacting the nanoparticles with a contact spot. This galvanic element generates a voltage or a current, which can be detected with the electronic circuits on the circuit surface.

Applicants further argue that the particles of the cited reference do not form the electrode of a galvanic element, whereas in the present invention nanoparticles form one of the electrodes of a galvanic element by enabling an electrical contact between that nanoparticle and the contact spot on the circuit surface. This argument has been fully and carefully considered but is not found to be persuasive. The claims require only

that a galvanic element is created and that 'an electrical property' is measured, where the breadth of these requirements can include the electrical detection of marker particles as a galvanic element, and measuring the resistance within a circuit is measurement of 'an electrical property'. The claims do not require the limitations as set forth in the argument or the cited portions of the specification, for example measuring voltage in the electronic circuit created by a current of positive charges from the counter electrode through the electrolyte to the nanoparticle as described in paragraph [44] of the specification. The specification further teaches the requirement of a potential between the nanoparticles and the counterelectrode (paragraph [45]) and the limitations in pairs of metals which may be used as nanoparticles and counterelectrodes (paragraphs [54]). The requirement that the galvanic element includes the contact spot and the counterelectrode (step (e) of claim 1) does not include any requirement for the nanoparticles to be included in the functional aspects of any created galvanic element beyond the presence of the nanoparticles establishing an electrical contact with the contact spot.

As such, the arguments traversing the application of the teachings of Knoll are arguments drawn to technical aspects which are disclosed in the specification, but not required by the instant claims.

Because the claims do not require the argued limitations, the following rejections are set forth and maintained.

Claim Rejections - 35 USC § 102

It is noted that the previous Office Action applied the teachings of Knoll only in a rejection of claims under 35 USC 103, where the claims required ‘covalently bound probe molecules’. The claims rejected in the instant rejection have been amended to require only ‘immobilizing probe molecules’ and does not specify any particular immobilization or bonding requirement.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5, 7, 8, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by over Knoll (1999; WO 99/27367).

This rejection is made using the publication date of PCT/EP98/07494. The publication is in German, thus the Examiner has relied upon the English translation provide by US Patent 6,548,311, which is a 371 from the aforementioned International application. Cited portions of the reference in this rejection are based upon the US Patent 6,548,311 publication column and line numbers.

Regarding claim 1, Knoll teaches providing a circuit surface with electronic circuits (see for example Fig 11 and 14), and specifically teaches an electrode that serves as a contact spot (e.g. Fig 10) and the requirement of a counterelectrode (e.g. col.7 ln.25) and that electrodes may be metal (col.11 lns.65-66) relevant to step (a), and providing immobilized probe molecules in spatial proximity to the circuits (see for example Fig 9 and 10), relevant to step (b). The reference teaches binding of metal nanoparticles (termed in the reference ‘marker particles’) to an analyte (Fig 10) (col.5

lns.53-61; col.13 ln.66 – col.14 ln.9), relevant to step (c), and binding of analyte molecules to the immobilized probe molecules (for example col.11 lns.10-12), relevant to step (d). Relevant to steps (e) and (f) , Knoll teaches (col.18 ln.30 – col.20 ln.5) that contact of an electroconductive marker to a potentiometric electrode allows ions to flow through an aqueous measuring medium (which is thus an electrolyte) to generate an electric current (thus forming a galvanic element) (relevant to step (e)) and that measuring an electrical property (col.9 ln.56; Abstract) enables the detection of analytes.

Regarding claim 4, Knoll teaches probe molecules bound to the circuit surface (for example Fig 10).

Regarding claims 7 and 8, Knoll teaches the marker particle bound to the analyte prior to binding of an analyte to a probe (Fig 9), relevant to claim 7, and nanoparticles with adhesion molecules (e.g. the reporter probe of Knoll is an adhesion molecule) attached to analyte molecules bound to surface bound probes (Fig 10) relevant to claim 8.

Relevant to claim 11, Knoll teaches that the marker particles may be conductive (col.14 lns.5-9), thus they are electrically conductive molecules.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Henkens et al (2002, US Patent 6,391,558).

As discussed in detail in the rejection of claims 1, 4, 5, 7, 8, and 11earlier in this Office Action, Knoll teaches all of the required limitations of Claim 1, from which claims 6, 18 and 19 depend.

Regarding claim 6, Knoll teaches probe molecules immobilized to an electrode surface, and analyte molecules affinity bound (e.g. antibody-antigen, Fig 5; DNA:DNA / probe:analyte hybridization) to the probe molecules.

Knoll does not particularly state that the immobilized probe (part 13 in Fig 10) is bound to the circuit surface by a covalent bond (claim 6), or provide any particular details regarding the binding of the marker particle (part 5 in Fig 9) to the analyte molecule (parts 11 and 11' in Fig 9) (claims 18 and 19).

Henkens et al teaches methods for the detection of nucleic acids using electrodes comprising immobilized probes, as well as analyte molecules labeled with detectable reporters.

Regarding claim 6 Henkens et al specifically teaches that capture probes may be covalently bound to an electrode (col.45 lns.16-25).

Regarding claims 18 and 19, Henkens et al teaches the PCR amplification of a analyte DNA molecule using primers modified at the 5' end, and gives the examples of fluorescein and biotin labeled primers (col.21 ln.60 - col 22. ln.4). Henkens et al indicates that the resulting labeled PCR product may be attached to a reporter molecule

by an interaction between the label from the PCR primer and a binding partner for the label of the primer. Relevant to claim 18, Henkens et al teaches the biotin:avidin binding pair, as well as labeling a PCR product using a biotinylated primer, and binding of the labeled PCR product to a avidin-gold biding partner (for example col.5 lns.25-35, col.43 ln.55). Relevant to claim 19, Henkens et al particularly teaches biding of a fluorescein-labeled PCR product to an anti-fluorescein HRP conjugate.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the nucleic acid probe immobilization methods of Henkens et al in the electrode based analysis methods of Knoll. One would have been motivated to do so based on the assertion of Henkens et al that covalent attachment of a probe is a preferred method (col.45 lns. 16-25). It would further have been obvious to use the probe:reporter binding method of Henkens et al to accomplish the marker particle:analyte binding of Knoll et al. One would have been motivated to do so because Henkens et al teaches that such methods can be used to attach a variety of different molecules (including colloidal gold which is similar to the description of marker particles by Knoll) to nucleic acid for analysis.

Claims 5 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Wohlstadter et al (2001, US Patent 6,207,369).

As discussed in detail in the rejection of claims 1, 4, 5, 7, 8, and 11 earlier in this Office Action, Knoll teaches all of the required limitations of claims 1 and 11, from which claims 5 and 12 depend.

Knoll does not specifically teach probe molecules bound to a countersurface positioned opposite the circuit surface (claim 5), or the use of polyene molecules to conduct an electrical signal (claim 12).

Regarding claim 5, Wohlstadter et al teaches methods of using several configurations of electrode-based devices in which the portion of the device where the analyte is collected (termed in the reference the 'binding domain') is on a surface opposite from an electrode (see for example Fig. 21 and Fig. 37).

Regarding claim 12, Wohlstadter et al teaches the use of a linking chain to ensure low resistance of electron transfer from the electrode, and specifically teaches the use of a polyacetylene chain (col.39 lns.53-63), which is on the polyene class.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have performed the electronic detection methods of Knoll using a probe binding area on a countersurface opposing an electrode. One would have been motivated to do so based on the teachings of Wohlstadter et al that in such a configuration the electrode can be protected during the binding reaction from the sample by a physical barrier that is subsequently removed thus, preventing contamination of the electrode surface which could result in a change in its electrochemical performance (col.64 lns.1-11). One would have a reasonable expectation of success because Wohlstadter et al teaches that the binding domain of the countersurface makes contact with the electrode and carries current from the counter electrode to the working electrode (col.45 lns.9-35). It would have been further obvious to use the polyacetlyene chains of Wohlstadter et al to ensure low resistance of

conductivity from the electrode to the marker particle as Wohlstadter et al teaches this use for polyacetylene chains.

Claims 13, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Fish (2002, WO 02/054052 A1).

As discussed in detail in the rejection of claims 1, 4, 5, 7, 8, and 11 earlier in this Office Action, Knoll teaches all of the required limitations of Claim 1, from which claims 6, 18 and 19 depend.

Relevant to claim 16, Knoll specifically teaches that the marker particles may be magnetic (see for example col.4 lns.10-24).

Relevant to claim 17, Knoll teaches that the marker particles may be dendrimers (col.14 lns.2-3), which are protrusions.

Knoll does specifically teach a requirement of nanoparticles touching a contact spot.

Fish teaches the detection of analytes using an electrode-based method wherein an opposing surface with an electrode is moved to make contact with an electrically readable particle that is bound to and analyte, where the analyte is bound to an immobilized probe (see for example Fig 1, p.14-18). Regarding claim 13, Fish specifically teaches that pressure is applied to the particle (p.16 last two lines) and that the bound particles make contact with the electrode (p.17 lns.7-8).

Regarding claim 16, Fish teaches that a countersurface may be moved in order to create a physical contact between an electrode (which is a contact spot) and an electrically readable particle, and also teaches that the probes may be attached to a contact spot and that movement of the countersurface causes the particles to make contact with the contact spot (see for example Fig 13 and page 28).

Additionally relevant to claim 17, Fish teaches that an electrode may be rough and have sharp edges and vertices to make electrical contact (p.42), thus teaching a circuit surface with electrically conductive protrusions.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have performed the electrode-based analyte detection method of Knoll by incorporating the countersurface movement taught by Fish to make contact between a particle and an electrode. One would have been motivated to do so based on the teachings of Fish that such methods allow accurate electrochemistry to be performed quickly at a low cost (p.7). One would have had a reasonable expectation of success because Knoll teaches that the electrode-based method can be used as a multi-step process separating the steps of particle transport and electrode binding (col. 5 lns.62-67).

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Fish (2002, WO 02/054052 A1), and further in view of Wohlstadter et al (2001, US Patent 6,207,369).

The teachings of Knoll in view Fish are applied to claim 14 as they were previously applied to claims 13, 16, and 17.

Knoll in view Fish teaches an electrode-based method of analyte detection wherein marker particles bind to analyte molecules and contact between the marker particle and a contact spot is made by the nanoparticles touching the contact spot.

Knoll in view of Fish does not specifically teach that the analyte molecule:particle complex is located on a surface opposite the circuit surface.

Wohlstadter et al teaches methods of using several configurations of electrode-based devices in which the portion of the device where the analyte is collected (termed in the reference the 'binding domain') is on a surface opposite from an electrode (see for example Fig. 21 and Fig. 37).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the opposed binding and electrode surfaces taught by Wohlstader et al in the electrode-based analyte detection method of Knoll in view of Fish. One would have been motivated to do so based on the teachings of Wohlstadter et al that in such a configuration the electrode can be protected during the binding reaction from the sample by a physical barrier that is subsequently removed thus, preventing contamination of the electrode surface which could result in a change in its electrochemical performance (col.64 lns.1-11).

Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knoll (1999; WO 99/27367) in view of Fish (2002, WO 02/054052 A1) and Wohlstadter et al (2001, US Patent 6,207,369), and further in view of Wang et al (2001).

The teachings of Knoll in view of Fish and Wohlstadter et al are applied to claim 15 as they were previously applied to claim 14.

Knoll in view of Fish and Wohlstadter et al teaches an electrode-based method of analyte detection wherein marker particles bind to analyte molecules which bind to probes on a surface opposite the circuit surface and contact between the marker particle and a contact spot is made by the nanoparticles touching the contact spot, as required by claims 13 from which the rejected claim 15 depends. Further relevant to claim 15, Knoll teaches that marker particles may be magnetic (see for example col.4 lns.10-24) and moved by a magnetic field (col.9 lns.22-25; Figs 16, 20 and 21), and that marker particles may be coated with metal (col14, lns.4-9). Relevant to claim 15, Wohlstadter et al teaches methods of using several configurations of electrode-based devices in which the portion of the device where the analyte is collected (termed in the reference the 'binding domain') is on a surface opposite from an electrode (see for example Fig. 21 and Fig. 37).

Knoll in view of Fish and Wohlstadter et al does not specifically teach that the linkage between the particle and the analyte molecule is broken.

Wang et al teaches an electrode-based method for the detection of an analyte (e.g. the detection of DNA hybridization). The reference teaches a method in which a gold nanoparticle binds to a target oligonucleotide wherein the target oligonucleotide

has hybridized to a probe oligonucleotide immobilized to a solid support (Fig 1; p.5577, left col., lns.5-10). The method of Wang et al includes a step of dissolution of the gold nanoparticle from the analyte molecule prior to detection of the gold nanoparticle at an electrode.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the dissolution of a gold microparticle from a bound analyte molecule as taught by Wang et al as a detectable nanoparticle in the electrode-based analyte detection method of Knoll in view Fish and Wohlstadter et al. One would have bee motivated to use such a method because Wang et al teaches the sensitivity ((p.5581, left col., lns.13-16) and adaptability (p.5581, right col., lns.17-19) of such a technique. Incorporating the methods of Wang et al into the teachings of Knoll et al would result in the use of a magnetic field to move an electrically conductive and magnetic marker particle to an electrode after separation of the particle from a particle:analyte:probe complex.

Conclusion

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Stephen Kapushoc
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